<u>REMARKS</u>

Claims 1-9 and 11-47 are pending in the application, of which Claims 16-47 have been withdrawn in response to a restriction requirement. Claims 1-9 and 11-15 have been examined and stand rejected. Claim 1 has been further amended to recite that the plasma-deposited temperature-responsive layer has a first layer and at least one second layer, where the first layer is deposited with a higher plasma power than the second layer. Support for this amendment is found in the original specification at page 25, lines 5-19 and in subsequent citations of this text at page 26, lines 3-8 and page 30, lines 22-26. Reconsideration and allowance of Claims 1-9 and 11-15 is respectfully requested.

<u>The Rejection of Claims 1-9, 11, and 14 Under 35 U.S.C. § 103(a) as Being Unpatentable Over Takei et al. (*Macromolecules*, 1994) in View of Carlson et al. (U.S. Patent No. 6,939,515)</u>

Claims 1-9, 11, and 14 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Takei et al. (*Macromolecules*, 1994) in view of Carlson et al. (U.S. Patent. No 6,939,515). This rejection is respectfully traversed. The Examiner characterizes Takei et al. as disclosing a temperature-responsive layer that can exist in a first state that binds living cells and can exist in a second state that binds less living cells and has relied on Carlson et al. as disclosing an assay device including a thermal platform that can support and controllably heat an array.

Takei et. al discloses a temperature-responsive material, poly(*N*-isopropylacrylamide) (pNIPAM), that, if functionalized (e.g., with a carboxyl group), can covalently bond to a specifically functionalized (e.g. amine-terminated) polymer surface. The pNIPAM disclosed by Takei et al. is deposited in solution (page 6164) and is limited to a single layer of polymer by the fundamental chemistry that drives the polymer-deposition process: a carboxyl group on the polymer reacts with an amino group on the polymer substrate surface (page 6165). Claim 1 has previously been amended to require that the temperature-responsive film be deposited by plasma

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deposition. Claim 1 has presently been amended to require that the plasma-deposited film be formed in at least two deposition steps, resulting in at least two layers: a first layer, deposited at a first high deposition power, that crosslinks and adheres to the second surface and at least one second layer, deposited at a second low deposition power, that can exist in a first state that binds molecules or living cells, and can exist in a second state that binds substantially less molecules or living cells than the first state. Given the singular nature of the temperature-responsive film disclosed by Takei et al., it is submitted that the at least two-layer devices of the claimed invention would not be obvious in light of Takei et al. when combined with Carlson et al.

The multistep-deposited plasma films of the present invention are distinct from those taught by Takei et al. As described in the application at page 25, lines 5-19, the use of at least two stages of plasma deposition has several advantages: the higher-power deposition activates the substrate and promotes adhesion of the polymer on the surface of the device and the lower-power deposition generates a film surface that retains the functionality of the monomer to a greater extent than the higher-power deposition. The substantial differences between the temperature-responsive films taught by Takei et al. and the present invention are further elucidated with the aid of two documents. The first supporting document, submitted herewith, is the declaration of Professor Buddy Ratner, Ph.D. (hereinafter "Ratner Declaration") and Professor Ratner's *curriculum vitae*. Second, submitted herewith, is X. Cheng et al. "Surface Chemical and Mechanical Properties of Plasma-Polymerized *N*-Isopropylacrylamide" *Langmuir* **2005**, *21*, 7833 (hereinafter "X. Cheng et al.").

The Ratner Declaration describes several essential differences between the multistep plasma-deposited films of the present invention and the films taught by Takei et al. Among the differences addressed in the Ratner Declaration are: the unique chemical structures of the higher- and lower-power deposition products for plasma-deposited pNIPAM; the solvent-less

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nature of plasma deposition versus the solution-based deposition taught by Takei et al. and how this enables greatly improved choices for compatible substrates; and the unexpectedly successful preservation of the temperature-responsive functionality of (monomer) NIPAM through the plasma-deposition process. Additionally, the Ratner Declaration describes experiments in which the chemical composition of plasma-deposited pNIPAM films deposited with multistep deposition and only high-power deposition are compared with the theoretical values for pNIPAM films. The experimental results indicate that the chemical composition of the different deposition-power films are different with respect to atomic species content and bonding content. These experimental results illustrate why a multistep plasma deposition process is important in producing films of the invention: the higher-powered deposition produces a heavily-crosslinked polymer that adheres to the substrate but lacks the temperature-sensitive functionality of a multistep deposition process that includes a low-power deposition step.

The Ratner Declaration unequivocally evidences the distinct properties and advantages of plasma-deposited pNIPAM films of the invention when compared to the solution-deposited films taught by Takei et al. While the materials of the invention and those taught by Takei et al. may be created from the same monomer (NIPAM), the subsequent processing and deposition through plasma (in the invention) and solvent (Takei et al.) yield films that have very different compositions and, as a result, properties. Of particular note in the Ratner Declaration is the stated unexpected result of creating a film that maintains the temperature-responsive qualities of the monomer (NIPAM) while creating a film that strongly adheres to a surface. This result is only possible when using the multistep plasma-deposition process of the invention that creates a strongly-crosslinked, but less-temperature-sensitive, foundation layer deposited at a higher deposition-power and a temperature-sensitive layer deposited with at least one lower deposition-power.

Further evidence of the distinction between the plasma-deposited films of pNIPAM of the present invention and the solution-deposited films of pNIPAM taught by Takei et al. can be found in X. Cheng et al., which provides an analysis of the differences and similarities between plasma-deposited pNIPAM (films of the present invention) and conventionally polymerized pNIPAM (films similar to those taught by Takei et al.). Plasma polymerization of pNIPAM taught by X. Cheng et al. is almost identical to that described in the present invention (compare X. Cheng et al., page7834 and application page 25, lines 5-19). Notably, X. Cheng et al. describes the results of mass spectrometry experiments that indicate a binary composition of films deposited with two different plasma-power levels: a heavily crosslinked (non-temperature responsive) and a monomer-containing (temperature responsive but not heavily crosslinked) species are detected (page 7836). An explanation is provided by the authors at the bottom of page 7836: low plasma-deposition power preserves monomer structure, whereas high power fragments and crosslinks monomers. The binary film composition is further described on page 7837: plasma-deposited films are described as having an "underlying adhesion-promoting layer formed during high-powered deposition" and a "top functional [plasma-deposited] pNIPAM coating."

The X. Cheng et al. reference also distinguishes plasma-deposited pNIPAM films as having a higher swelling ratio and elastic modulus, both above and below the lower critical solution temperature (LCST), than traditionally synthesized pNIPAM (page 7839). This difference is attributed to a greater degree of crosslinking in plasma-deposited pNIPAM films (*id.*), such as those of the present invention.

The present application, the Ratner Declaration and the X. Cheng et al. reference each confirm the unique and distinct composition of films of the present invention when compared to the films described in the Takei et al. reference. Carlson et al. does nothing to remedy the

deficiencies of the disclosure of Takei et al. in this regard. Because of the above-described unique characteristics of the plasma-deposited temperature-responsive films of the invention, it is submitted that the devices of the claimed invention would not be obvious in light of Takei et al. when combined with Carlson et al.

In view of the above, Claim 1, and Claims 2-9, 11, and 14 which depend therefrom, could not have been obvious over Takei et al. in view of Carlson et al. Accordingly, the Examiner is respectfully requested to withdraw this ground of rejection.

<u>The Rejection of Claims 12, 13, and 15 Under 35 U.S.C. § 103(a) as Being Unpatentable over Takei et al. (*Macromolecules*, 1994) in View of Carlson et al. (U.S. Patent No. 6,939,515), in Further View of Lahann et al. (U.S. Patent No. 7,020,355)</u>

Claims 12, 13, and 15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Takei et al. (*Macromolecules*, 1994) in view of Carlson et al. (U.S. Patent No. 6,939,515), in further view of Lahann et al. (U.S. Patent No. 7,020,355). Claims 12, 13, and 15 depend directly or indirectly from independent Claim 1. The Examiner builds upon the previous rejection of Claim 1 (based on Takei et al. in view of Carlson et al.) by citing Lahann et al. as further disclosing the use of assays using proteins and antibodies. It is submitted that Takei et al. and Carlson et al. do not combine to render Claim 1 obvious for the reasons given above. The addition of the teachings of Lahann et al. does not cure any of these defects and thus does not render Claims 12, 13, and 15 obvious within the meaning of 35 U.S.C. § 103(a).

In view of the above, it is demonstrated that the combination of Takei et al., Carlson et al., and Lahann et al. fail to teach, suggest, provide motivation to make, or otherwise render obvious the invention of Claims 12, 13 and 15. Accordingly, applicants respectfully request removal of this ground of rejection.

Conclusion

In view of the foregoing amendments and comments, it is believed that amended Claims 1-9 and 11-15 are in condition for allowance. Reconsideration and favorable action is requested. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone applicants' attorney at the telephone number set forth below.

Respectfully submitted,

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